Electron-transfer Chain (ETC) Promotion of Aromatic Substitution Reactions. Entry into the $S_{ON}2$ Mechanism *via Ipso* Radical Attack

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Summary The oxidative electron-transfer chain mechanism, the $S_{ON}2$ mechanism, is shown to be initiated by benzoyloxyl radicals since 4-fluoroanisole can be converted into a mixture of 4-methoxyphenyl acetate and benzoate (maximum ratio 10:1) in high yield by decomposing benzoyl peroxide in HOAc–KOAc at 78 °C.

THE $S_{ON}2$ mechanism is a member of the family of electron-transfer chain-(ETC) promoted processes,[1] of which the $S_{RN}1$ variety is the best established one so far.[2] For an aromatic substrate (ArX), the $S_{ON}2$ mechanism† consists of an initial one-electron oxidation step (1) followed by *ipso* attack of a nucleophile on the radical cation formed [step (2)], and loss of X^- to give a new radical cation [step (3)]. The chain-transfer step is the oxidation of ArX by this radical cation [step (4)].

$$\mathrm{ArX} \rightarrow \mathrm{ArX}^{\cdot+} \qquad (1)$$

$$\mathrm{ArX}^{\cdot+} + \mathrm{Nu}^- \rightarrow [\mathrm{ArXNu}]^{\cdot} \qquad (2)$$

$$[\mathrm{ArXNu}]^{\cdot} \rightarrow \mathrm{X}^- + \mathrm{ArNu}^{\cdot+} \qquad (3)$$

$$\mathrm{ArNu}^{\cdot+} + \mathrm{ArX} \rightarrow \mathrm{ArNu} + \mathrm{ArX}^{\cdot+} \qquad (4)$$

We recently showed[4] that the 'oxidative' substitution of 4-fluoroanisole by acetate ion in HOAc to give 4-acetoxyanisole is indeed 'catalytic in positive holes,' each hole giving rise to 2·7 molecules of product. It was also pointed out that another possible entry into the $S_{ON}2$ mechanism would be step (5), *ipso* attack by $\mathrm{Nu}^{\cdot}$ on the parent compound, ArX, instead of step (2). A possible case of such a reaction might

$$\mathrm{ArX} + \mathrm{Nu}^{\cdot} \rightarrow [\mathrm{ArXNu}]^{\cdot} \qquad (5)$$

be the attack of pentafluorobenzoyloxyl radical on chloro- and bromo-benzene to give relatively high yields (40—50%,

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† What might be an intramolecular version (S_{ON}i), the $\mathrm{Rh^{III}}$ catalysed cyclization of 3-(*o*-fluorophenyl)propan-1-ol to form chroman, has recently been reported.[3]

based on the amount of PhCOO·) of phenyl pentafluorobenzoate.[5]

We now can demonstrate that this type of reaction occurs with high efficiency, again using 4-fluoranisole as a model compound (we prefer fluorine as a leaving group at present to avoid discussion of the possibility that it might depart as F· or F$^+$). Since the acetoxyl radical is highly unstable toward decarboxylation[6] (E_a *ca.* 7·5 kcal mol^{-1})‡ benzoyl peroxide was chosen as a source of acyloxyl radicals, whereas acetate ion was retained in the role of Nu$^-$. This has the advantage that the radical-chain length can be estimated (see below).

Table. Substitution of 4-fluoroanisole (ArF) in HOAc–KOAc in the presence of decomposing benzoyl peroxide.[a]

		Yield/%[b]		
Expt.	$(PhCOO)_2$/ mmol	ArOAc	ArOCOPh	Other products[c]
1	0·25	41	16	12
2	0·5	65	20	10
3	1	88	12	11
4[d]	1	65	18	14
5[e]	1	78	12	12
6	2	54	10	9
7[f]	1	10	12	10
8[g]	1	6	10	8
9[h]	1	57	6	7

[a] Reaction conditions, unless otherwise stated: [Substrate] = 1 M, glacial acetic acid, [KOAc] = 0·5 M, acetic anhydride added (to remove water) together with the peroxide. *T*, 78 °C. [b] G.l.c. yield based on PhCOO·. [c] Fluoromethoxybiphenyls and fluoromethoxyphenyl benzoates. [d] [Substrate] = 2 M. [e] [KOAc] = 1 M. [f] No acetate ion present. [g] No acetate ion present and trifluoroacetic acid (50 μl) added. [h] KF (2 mmol) added.

The Table gives yields of products from the decomposition of benzoyl peroxide in the presence of 4-fluoroanisole in acetic acid with or without acetate ion present. In the presence of acetate ion (expts. 1—6) the predominant products are those of *ipso* substitution of fluorine, namely 4-methoxyphenyl acetate and benzoate in a ratio of 2·6—7·3: 1 with small amounts of other products (those expected from normal benzoyloxyl radical chemistry,[7] namely fluoromethoxybiphenyls and fluoromethoxyphenyl benzoates). Total yields in excess of 100% (based on PhCOO·) demonstrate the 'catalytic' nature of the reaction. In the absence of acetate ion (expt. 7), the yield of the benzoate remains approximately constant whereas the acetate yield decreases strongly. Suppression of the auto-ionization of HOAc by adding a trace of trifluoroacetic acid further decreases the yield of the acetate (expt. 8). Addition of fluoride ion from an external source to the reaction medium caused an increase of the acetate to benzoate ratio to *ca.* 10: 1 (expt. 9). Blank experiments showed that 4-methoxyphenyl benzoate is completely stable under the reaction conditions employed.

These results are best interpreted with step (5) as the initial step (Nu· = PhCOO·). The fluorobenzoyloxycyclohexadienyl radical loses fluoride ion [step (3)] and the 4-benzoyloxyanisole radical cation starts a radical chain-reaction [step (4)] involving maximally 10 cycles of steps (2) to (4), forming 4-methoxyphenyl acetate. With no acetate ion present, the chain reaction cannot be sustained by the much weaker nucleophile, HOAc, and we see predominantly normal benzoyloxyl radical chemistry.

Apart from the pentafluorobenzoyloxyl radical reaction referred to above,[5] similar substitutions of aromatically bound fluorine and chlorine have been noticed earlier, *e.g.*, in the radical aroyloxylation of perfluoroaromatics[8] and in the photochemical benzoyloxylation of chlorobenzene to give phenyl benzoate.[9]

Financial support from the Swedish Natural Science Research Council is gratefully acknowledged.

(*Received*, 10*th November* 1980; *Com.* 1211.)

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‡ 1 cal = 4·184 J.

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